REMARKS

Applicants respectfully requests entry of the amendments and remarks submitted herein. Claims 1 and 7 have been amended to recite a "purified or isolated" protein. Support for this amendment can be found in Applicants' specification at page 11, lines 5-27, which provides a definition for "purified" or "isolated" polypeptides. Claim 1 has been further amended to recite that the molecular weight of the 55 kD protein is determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) under reducing conditions. Support for this amendment can be found in Applicants' specification at, for example, page 78, lines 11-16, which disclose that samples were suspended in Tris-SDS and separated on a SDS 12% to 4% polyacrylamide gradient gel. Claim 15 has been amended to incorporate the language of amended claims 1 and 7. Claim 59 has been canceled. Thus, claims 1, 7, 15, 21, and 23-25 are pending. No new matter has been added.

In light of the amendments and the following remarks, reconsideration and allowance of claims 1, 7, 15, 21, and 23-25 is respectfully requested.

Interview summary

Applicants' agents thank the Examiner for the courtesy of a telephonic interview on June 30, 2004. During the interview, the outstanding Office Action and potential claim amendments were discussed.

Rejections under 35 U.S.C. § 101

The Examiner maintained the rejection of claim 1 under 35 U.S.C. § 101 as being directed to non-statutory subject matter, as set forth in the previous Office Action. In the previous Office Action, the Examiner stated that the claimed polypeptide has the same characteristics as that found in nature. Applicants amended claim 1 to recite "a purified protein" in the response filed February 2, 2004. In the current Office Action, the Examiner stated that the rejection is maintained because the limitation "isolated" is not set forth in the claim. The Examiner also rejected claim 7 under 35 U.S.C. § 101 as being directed to non-statutory subject matter.

The following definition is set forth in the specification at page 11, lines 5-24:

> . . . an "isolated" or "purified" polypeptide is a . . . polypeptide that exists apart from its native environment and is therefore not a product of nature. An isolated . . . polypeptide may exist in a purified form or may exist in a non-native environment such as, for example, a transgenic host cell. For example, an "isolated" or "purified" . . . protein . . . is substantially free of other cellular material . . .

Given this definition, a person having ordinary skill in the art would understand that a "purified" protein as recited in present claims 1 and 7 is not the same as a protein found in nature. A person of ordinary skill also would understand that a "purified" protein and an "isolated" protein are essentially the same. To further prosecution, Applicants have amended claims 1 and 7 to recite a "purified or isolated" protein. Thus, it is clear that the claimed molecules are not naturally-occurring.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1 and 7 under 35 U.S.C. § 101.

Rejections under 35 U.S.C. § 102

The Examiner maintained the rejection of claims 1, 15, 21, and new claim 59 under 35 U.S.C. § 102(b) as being anticipated by Fraser *et al.* (1999) Accession Number AAY 75751, as set forth in the previous office action. Specifically, the Examiner stated that the Fraser *et al.* reference discloses a novel *N. gonorrhoeae* polypeptide having an amino acid sequence that is 98.2% similar to SEQ ID NO:4. The Examiner further stated that this reference discloses that the polypeptide could be used as a vaccine, an immunogenic composition, or to raise antibodies. Thus, the Examiner concluded that the Fraser *et al.* reference anticipates the presently claimed invention.

As amended, claim 1 recites an isolated or purified 55 kD protein wherein the molecular weight is determined by SDS-PAGE under reducing conditions. Amended claim 7 recites an isolated or purified protein containing the amino acid sequence of SEQ ID NO:4. As amended, claim 15 recites a vaccine containing a protein as recited in claim 1 or claim 7. The Fraser *et al.* reference does not disclose all of the features of the present amended claims. Rather, the Fraser *et al.* reference provides only an amino acid sequence encoded by an *N. gonorrhoeae* open

reading frame. At no point does the Fraser *et al.* reference disclose isolation or purification of a polypeptide having the discloses amino acid sequence. Further, the Fraser *et al.* reference does not disclose the molecular weight of the polypeptide as determined using SDS-PAGE or any other method. Moreover, the amino acid sequence of the Fraser *et al.* reference is not SEQ ID NO:4. As such, the Fraser *et al.* reference does not anticipate the present claims.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 15, and 21 under 35 U.S.C. § 102(b).

The Examiner also maintained the rejection of claims 1, 7, 15, and new claim 59 under 35 U.S.C. § 102(a) as being anticipated by Parkhill *et al.* (2000) Accession Number B81859, as set forth in the previous office action. Specifically, the Examiner stated that the Parkhill *et al.* reference discloses a novel *N. meningitidis* polypeptide with an amino acid sequence that is 100% identical to that set forth in SEQ ID NO:4. The Examiner further stated that characteristics such as a molecular weight of 55 kD is considered to be an inherent property of the polypeptide disclosed in the Parkhill *et al.* reference. Thus, the Examiner concluded that the Parkhill *et al.* reference anticipates the present invention.

Applicants assert that the Parkhill *et al.* reference does not teach the claims as presently amended. The Parkhill *et al.* reference cited by the Examiner merely sets forth the amino acid sequence of a putative protein. Moreover, the *Nature* article corresponding to the cited Parkhill *et al.* reference merely discloses that the complete genomic sequence of a particular strain of *N. meningitidis* was obtained and compared with sequences in the EMBL database to identify potential open reading frames. Neither of these references discloses purification or isolation of any *N. gonorrhoeae* protein, as recited in amended claims 1 and 7. These references also fail to disclose the molecular weight of the protein as determined by SDS-PAGE under denaturing, non-reducing conditions, as recited in amended claims 1 and 15. Further, the Parkhill *et al.* references fail to disclose the use of the protein in a vaccine as recited in claim 15. As such, the cited Parkhill *et al.* reference does not anticipate the present claims.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 7, and 15 under 35 U.S.C. § 102(a).

Rejections under 35 U.S.C. § 112

The Examiner rejected claims 1, 7, 15, 21, 23-25, and 59 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. With respect to claims 1, 7, and 15, the Examiner stated that the recitation of "55 kD" is vague and indefinite in view of the discrepancies encountered in the art when molecular weights are determined by different methods. With respect to claims 7 and 59, the Examiner also stated that it is not possible to determine whether Applicants are claiming the amino acid sequence of SEQ ID NO:4 or another sequence that contains the amino acid sequence of SEQ ID NO:4.

Applicants have removed the term "p55" from claims 1, 7, and 15. In addition, Applicants have amended claim 1 to recite a protein comprising a 55 kD polypeptide wherein the molecular weight is determined by SDS-PAGE under reducing conditions. Applicants also have amended claim 7 to recite a protein comprising the amino acid sequence of SEQ ID NO:4. Moreover, Applicants have amended claim 15 to recite a vaccine comprising the polypeptide or protein as recited in claim 1 or claim 7. Thus, the present claims are clear and definite.

In light of these amendments, Applicants respectfully request withdrawal of the rejections of claims 1, 7, 15, 21, and 23-25 under 35 U.S.C. § 112, second paragraph.

The Examiner also maintained the rejection of claims 15 and 21 and new claim 59 under 35 U.S.C. § 112, first paragraph, for lack of enablement as set forth in the previous Office Action. The Examiner stated that the Declaration submitted in response to the previous Office Action was not persuasive, because it did not address the issue of whether a vaccine containing the claimed polypeptide would block invasion of *N. gonorrhoeae in vivo*. The Examiner further stated that while the specification discloses the claimed composition and general methods for formulating compositions in pharmaceutically acceptable carriers, there is insufficient guidance that would enable a person of ordinary skill in the art to use the claimed compositions as vaccines against *N. gonorrhoeae*. Finally, the Examiner alleged that undue experimentation would be required for a person reading the specification to use the claimed composition for the prevention, treatment, or cure of a disease, because no basis is provided upon which to determine or predict an amount of the composition that would be effective for the intended use.

It is well established that there is no art-accepted animal model for human gonococcal infection, even though researchers have attempted to generate an effective animal model for the disease. See, for example, the Cohen and Cannon reference (*J. Infect. Dis.* (1999) 179(Suppl. 2):S375-S379; copy attached), which teaches that there is no valid experimental animal model that might be useful to develop a gonorrhea vaccine. This reference also discloses that experimental gonorrhea cannot be pursued in women due to the likelihood of complications.

Since experimental gonorrhea cannot be studied in women, primary cervical cells are an art-accepted system in which to evaluate the potential immunogenic use of *N. gonorrhoeae* proteins. Primary cervical cells are an established *ex vivo* model system for evaluating gonococcal infection, and have been used to generate data that is sufficient to support the present claims. In fact, in the application and in the Declaration under 37 C.F.R. § 1.132 that was filed with the response to the previous Office Action, Applicants used primary human cervical cells to show that the p55 protein of *N. gonorrhoeae* is involved in modification of the cell membrane to enhance entry of the gonococcus. These experiments also established that p55 can be used to raise antibodies and thus provide protective immunity by interfering with gonococcal infection. As such, Applicants' use of this *ex vivo* model system clearly provides support for the effectiveness of p55 to provide protective immunity by interfering with gonococcal infection.

Applicants note that immunization relates to the induction of an immunological response, but does not necessarily require complete immunological protection. This is stated in Applicants' specification at, for example, page 45, line 28 to page 46, line 1, which teaches that an effective amount of an active ingredient in a vaccine "is sufficient to prevent, ameliorate, or reduce the incidence of *N. gonhorrhoeae* colonization in the target mammal." In addition, the specification at page 2, lines 13-26 teaches that methods of vaccination effective to immunize a patient against *N. gonorrhoeae* can prevent, ameliorate, or reduce the incidence of gonorrhea. Thus, the vaccines of the invention are not required to completely prevent all gonorrheal infection in an immunized subject.

Applicants also submit that the teachings of the specification, in combination with the level of skill in the art at the time the application was filed, would have enabled the use of the claimed polypeptides in vaccines against *N. gonorrhoeae*. For example, Applicants' specification at page 43, lines 11-23 teaches that *N. gonorrhoeae* polypeptides can be used in

vaccines. This section of the specification also teaches that combining an *N. gonorrhoeae* polypeptide with a vehicle, an adjuvant, or a carrier can be useful. In addition, the section of Applicants' specification extending from page 45, line 24 to page 46, line 26 teaches methods for administering a vaccine to a subject, as well as methods for preparing a vaccine. For example, this section of the specification discloses that neisserial proteins can be administered parenterally, orally, or via a mucosal route, and may be combined with a vehicle and/or an adjuvant.

In addition, the section of the specification extending from page 49, line 11 to page 54, line 2 discloses methods for formulating and administering compounds to a subject. For example, this section teaches that compounds can be formulated as pharmaceutically acceptable salts using standard procedures. This section of the specification also teaches that pharmaceutical compositions can be administered to a mammal by a variety of routes, including orally, intravenously, topically, or subcutaneously. Moreover, the specification at page 53, lines 10-25 discloses that suitable doses can range from about 0.5 mg/kg to about 100 mg/kg body weight per day, preferably from about 10 to about 75 mg/kg/day, more preferably from about 6 to about 90 mg/kg/day, and most preferably from about 15 to about 60 mg/kg/day. Specific dosage amounts are not disclosed and, Applicants submit, are not required, since amounts will vary depending on the particular compound, the route of administration, and the age and condition of the recipient (see specification at page 53, lines 5-9).

Further, Applicants respectfully submit that the relative skill of those in the art at the time the application was filed can be characterized as being quite high. Those skilled in the art at the time Applicants filed the present application can be considered scientists who understood the problems associated with human infection by *N. gonorrhoeae*, the lack of a suitable animal model therefor, and the vast possibilities for immunization against *N. gonorrhoeae* once a suitable immunogen was identified. Clearly, a person skilled in the art would have been well aware of the types of experiments needed to determine whether a neisserial polypeptide such as p55 would be useful in a vaccine to immunize a subject against gonorrhea. For example, Applicants submit that a person of skill in the art would have been able to perform well-known biochemistry, molecular biology, and/or immunology techniques such as recombinant protein expression, protein purification, and generation and characterization of antibodies. A person of

skill in the art also would have been able to determine a suitable dose of vaccine to administer to a particular subject. Thus, Applicants respectfully submit that given the teachings of the specification and the level of skill in the art, a person having ordinary skill in the art, reading Applicants' specification at the time the application was filed, would have been able to make and use the presently claimed vaccine without undue experimentation.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 15 and 21 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In light of the above, Applicants submit that claims 1, 7, 15, 21, and 23-25 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone the undersigned if such would further prosecution.

Applicants believe that no fees are due. Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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